

Risk Stratification for Cardiac Arrhythmia Patients

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Final Report

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Summary Contributions:

- An accurate, physician-friendly, postoperative AF risk stratification system that performs even under missing data conditions, while outperforming the “state of the art” system,
- A thorough analysis of previously examined and novel pre- and postoperative clinical and ECG features for postoperative AF risk stratification,
- A new methodology for genetic algorithm-built traditional Bayesian network classifiers allowing dynamic structure through novel chromosome, operator, and fitness definitions, and
- An integrated methodology for inclusion of doctor’s expert knowledge into a probabilistic diagnosis support system.

Research

Currently, roughly thirty percent of coronary artery bypass graft (CABG) patients develop atrial fibrillation (AF) in the five days following surgery, increasing the risk of stroke, prolonging hospital stay three to four days, and increasing the overall cost of the procedure[1, 2]. According to some studies, over \$1 billion is spent annually on this problem in the US alone [1]. Current pharmacologic and nonpharmacologic means of AF prevention are suboptimal, and their side effects, expense, and inconvenience limit their widespread use [3]. An accurate method for identifying patients at high risk for postoperative AF would allow these methods to be focused on the patients where its utility would be highest.

Several identification approaches have been proposed for this purpose, but results have been unimpressive [1-22]. Most clinical studies investigate a relatively small amount of measurements and/or variables after a significant amount of time and money have been invested. Then, simple univariate and multivariate techniques are used that can miss possible correlations between variables that may hold the answer to the problem. By simply collecting more data types and using more intelligent feature selection and classification techniques, we could shed more light on the problem being investigated.

This work illustrates the problem with the traditional approach and proposes a novel method for the creation of better classifiers based on the data that are already collected in many hospitals across the country. We present and test this method in this work and evaluate a methodology of electrocardiogram/electrogram (ECG) feature extraction to contribute to the risk stratification of AF following coronary bypass graft.

Objectives

The main objective of this research was to develop Bayesian networks (BN) and possibly other classifiers which could model/predict/assign risk of the occurrence of AF in CABG patients through the incorporation of different types of patient data. Clinical data and ECG derived features, both traditional and novel, are selected and combined using an evolutionary computing algorithm. We investigate profit or loss due to the inclusion of the following data types:

- Clinical Data: Risk factors and other medical indicators currently recorded in the hospital after CABG and
- ECG Features: Time, frequency, and wavelet domain features derived from the collected ECG signals showing AF prediction potential.

A secondary objective was to develop an integrated framework for more advanced methods of feature selection and fusion for medical classification/prediction. To validate this novel methodology, we compare current methods of data investigation to more advanced methodologies, specifically genetic programming and BNs.

Methods

Clinical data and ECG have been collected in two separate studies. The first, performed at the Hospital of the University of Pennsylvania, collected clinical data and ECG recordings following CABG and monitored which of these patients developed AF. The second study was performed at the Atlanta Veterans Affairs Medical Center, where presurgical ECGs were collected along with other clinical variables. Both studies are approved by each institution's respective Institutional Review Boards (IRB). ECG features include separation of the ECG into its individual waveforms with further analysis of these components, including wavelet, spectral, and time domain features. Using these two sets of data, characteristics of the ECG, as well as the clinical variables, are investigated singly and in combination to find their relationship to the onset of AF following CABG. Multivariate classifiers are created by selecting features with a genetic algorithm (GA) and by combining the variables using logistic regression or a BN. These classifiers are then validated and their results analyzed and compared.

Contributions

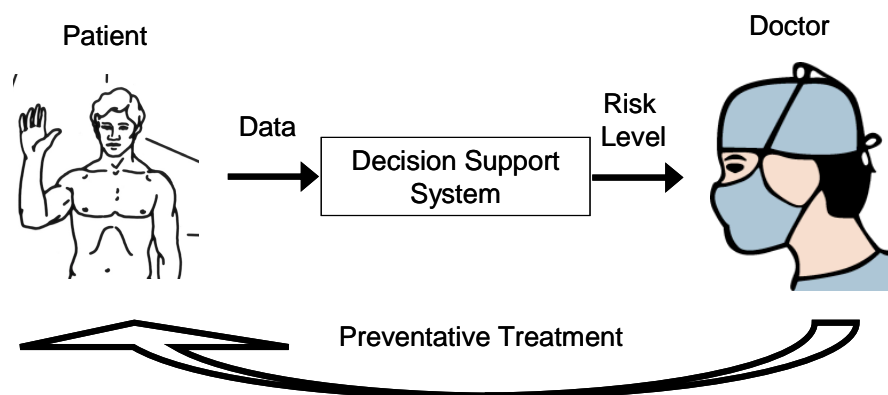


Figure 0.1 Block diagram of AF risk stratification system including the patient, the decision support system, and the cardiologist.

In order to more effectively prevent AF in CABG patients, high-risk patients must be identified and treated prophylactically through pharmacological or pacing means [3]. The overall system level approach to the control of postoperative AF consists of the patient, the decision system, and the physician that, based on the outcome of the decision system, prescribes the treatment. The contributions of this research focus on the decision system in this progression. The patient identification and treatment feedback control loop lends itself well to the application of intelligent control, possibly using automatic drug administration or electrical stimulation, though its implementation is beyond the scope of this research, due to the uncertainty behind the exact characteristics of these treatments. Contribution of this research to the decision system specifically includes:

- An accurate, physician-friendly, postoperative AF risk stratification system that performs even under missing data conditions, while outperforming the “state of the art” system,
- A thorough analysis of previously examined and novel pre- and postoperative clinical and ECG features for postoperative AF risk stratification,
- A new methodology for GA-built traditional BN classifiers allowing dynamic structure through novel chromosome, operator, and fitness definitions, and
- An integrated methodology for inclusion of doctor’s expert knowledge into a probabilistic diagnosis support system.

Important medical problems have been “poked at” with limited feature selection/fusion methods for much too long, especially while there are advanced methods of data mining and decision-making to be applied. The BN is an excellent tool for making decisions based on collected information, and is even able to handle missing data points [23]. By combining more types of data and expert knowledge into a BN, better accuracy and healthier patients are the likely result.

Summary of Research Findings

This work has presented univariate and multivariate risk stratification routines in the form of:

- A single variable,
- GA feature-selected multivariate logistic regression,
- GA feature-selected k -Nearest Neighbor,
- GA feature-selected naïve BN,
- Greedily-built (K2 method) traditional BN, and
- GA learned structure and feature-selected traditional BN.

Of the univariate predictors, it seems that the patient’s age is the most reliable, as well as the best recognized. Unfortunately, this does not offer the sensitivity or specificity needed for making clinical decisions. The multivariate logistic regression seems to be prominent in the literature and has worked well in our experiments when the features are selected by GA. The k -NN actually performed slightly better than regression in terms of fitness, though this method requires the loading of all training points into memory to perform tests, a significant problem when dealing with high dimensional, large dataset problems. Additionally, the cluster theory that the k -NN is based on has not gained acceptance with

clinicians who seem to prefer regression or probability models. The traditional BNs were particularly useful in the ECG datasets when it was offered a large number of features. Overall, the GA feature-selected naïve BNs performed the best while offering other superior qualities that allow easy of use and robustness to clinical situations. Specifically, the naïve BN built using preoperative clinical data had the best combination of performance and usability. For instance, BNs are based on probabilities of previous AF patients' data. This is similar to how a cardiologist might use their past experience to make decisions. Additionally, naïve BNs require less data to populate their probability tables due to their independent conditional probability assumptions. Since BNs perform inference probabilistically, physicians can use this classifier when some of the inputs have missing values. This is not possible with classifiers such as multivariate regression or k -NN. As we saw in chapter four, these classifiers discarded sometimes more than half of the patient population when finding the optimum feature subset. The BNs, on the other hand, always used all the patient data it was presented with and returned a comparable fitness.

Suggested Follow-up Work

One of the main obstacles to the ECG analysis of the datasets is the lack of automated ECG annotation. Though there are certainly systems which do this in the hospital, these were not available for this work. A greater volume of quality ECG recordings and annotations would allow much more advanced feature extraction routines to be performed, including various machine learning techniques.

Though we have investigated many types of BNs in this study, there are a number of questions that need to be better understood to advance the use of these systems in a decision support role in medicine. We urge the use of these systems with larger sets of data, especially datasets that were collected in the hospital. In this way, missing data would appear as it naturally would instead of in a simulated manner. This would allow the BN to “learn” what missing values happen in what circumstances, allowing it to tailor itself to the best possible predictions in realistic cases.

Larger datasets would also allow a number of other interesting investigations. In this work, we were limited by the number of levels we could discretize the data because if we allowed more than binary, this increases the size of the joint probability tables, thereby requiring more data points to create accurate probability estimates. We think a more varied discretization scheme for some interesting variables (*i.e.* age, left atrial volume, ejection fraction, etc.) could yield additional predictive information.

Traditional BNs also perform best with large amounts of data and we think with a larger dataset, the traditional BNs might have been the best classifier, but this cannot be verified until a larger dataset is analyzed.

An interesting topic would be the resolution of the probability shifting that occurs when using LOO validation as we saw in chapter five. This might be resolved through a probability correction term in the fitness function indicating the number of patients used and discarded. This same type of approach might also be applied to the K2 greedy BN building method to cure its selection of variables with few patient samples.

Lastly, we suggest the use of these methods of GA feature selection in naïve BNs and GA structure learning and feature selection for traditional BNs to be used in other medical fields. Their flexibility, robustness, and accuracy make them ideal for use in real world applications and we feel this methodology lends itself well to a wide range of risk stratification needs present in the medical community.

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